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10/679,052	10/03/2003	Archie B. Williams III	048777/277097	7084

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EXAMINER	
SCHLIENTZ, LEAH H	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/679,052	Applicant(s) WILLIAMS, ARCHIE B.	
	Examiner Leah Schlientz	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/29/07 and 3/9/07*.
2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-85* is/are pending in the application.
4a) Of the above claim(s) *13,14,28,46,47,49-61,71-73 and 75* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1-10,12,15-27,29-45,48,62-70,74 and 76-85* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a)☐ All b)☐ Some * c)☐ None of:
1.☐ Certified copies of the priority documents have been received.
2.☐ Certified copies of the priority documents have been received in Application No. _____.
3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement of Receipt

Receipt of Applicant's Response, filed 01/29/2007, in response to the Office Action mailed 8/7/2006, is acknowledged and has been entered. Claims 1 – 10 and 12 – 85 are pending, of which claims 13, 14, 28, 46, 47, 49 – 61, 71 – 73, 75 are withdrawn from consideration as being drawn to non-elected species. Claims 1 – 10, 12, 15 – 27, 29 – 45, 48, 62 – 70, 74 and 76 – 85 are readable upon the elected invention.

Response to Arguments

Applicant's arguments filed 1/29/2007 with regard to the rejection of claims 3 – 4, 27, 29, and 33 under 35 USC 112, second paragraph, have been fully considered and are persuasive. The rejection of claims 3 – 4, 27, 29, and 33 has been withdrawn as having been overcome by amendment. The arguments with regard to claim 34 has been considered, but is not fully persuasive. The response on page 12 recites that the claim has been amended to read "a diagnostic procedure wherein the diagnostic procedure comprises imaging at least a portion of the individual's gastrointestinal tract," however, it appears that no amendment as such has been made. Claims 34 – 44 stand rejected for reasons set forth in the Office Action mailed 8/7/2006.

Applicant's arguments filed 1/29/2007 with regard to the rejection of claims 1 – 7, 11, 12, 15, 16, 20 – 22, 34 – 41, 45, 48, 62 – 67, 69 and 70 under 35 USC 102(b) or (e) as being anticipated by Ramm, Nyman, Johnson, Zeman, or Gore, have been fully considered. The rejections have been withdrawn as having been overcome by amendment.

Applicant's arguments filed 1/29/2007 with regard to the rejection of claims 1 – 12, 15 – 27, 29 – 45, 69, and 70 under 35 USC 103(a) as being upatentable over Widder in view of Fuisz in further view of Nyman have been fully considered and are persuasive. The rejection of claims have been withdrawn because Widder fails to teach a barium-containing contrast agent, rather teaches an alternative material as a low density contrast material. Likewise, the rejections of claims 1 – 6, 11, 12, 15 – 21, 34 – 45, 48, and 62 – 64 as being unpatentable over Widder in view of Balthazar, and the rejection of claims 1 – 6, 11, 12, 15 – 21, 34 – 45, 48, 62, 63, and 68 as being unpatentable over Widder in view of Ha have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8 and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. While the specification, as originally filed, shows certain specific amounts of barium such as 0.01%, 0.02%, 0.03%, etc., it does not show support for the full range of concentrations from about 0.01 to about 0.2% w/v. This is a new matter rejection.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34 – 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims as written are ambiguous because it is unclear what diagnostic procedure Applicant is referring to. Please clarify in order that one may readily ascertain what is being claimed. For example, the action stated in step (b) does not clarify which type of diagnostic procedure that is performed. There are a multitude of potential "diagnostic" procedures which can be performed on a subject and thus the nature of the claimed diagnostic procedure which is to be performed is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

> granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 – 7, 12, 15 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Falasch *et al.* (DD 23830 (abstract)).

Falasch discloses $BaSO_4$ suspensions for x-ray diagnostics which are stabilized with clay in aqueous solutions. Barium sulfate represents from 0.5 to 2.0% of the compositions. The compositions also contain from 3 – 6% clays, sweeteners and flavors. The compositions are inexpensive and provide good sedimentation stability, contrast properties and physiological acceptability (abstract). Regarding claims 1 – 5, Falasch *et al.* do not disclose a Hounsfield value, however the Hounsfield value is an inherent property of a given contrast agent, and in the absence of evidence to the contrary, the stated barium sulfate-containing contrast agent is of suitable concentration to be expected to have a Hounsfield value within the claimed ranges. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1 – 7, 12, 15, 17, 18, 34 – 41, 45, 46, 48, 62 – 64, 70, 54 and 76 – 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Tait *et al.* (US 2001/0036442).

Tait discloses a stool marker for oral administration and suitable for use in CT colography (abstract). The formulation is used in a method of radiologically visualizing the colon of a patient including the steps of orally administering the marker, radiologically scanning the colon of a patient, and manipulating data to determine the portion of data due to marked stool to thereby provide a representation of the colon, including where present, a polyp (paragraphs 0023 – 0026). Barium sulfate is present in the formulation in an amount ranging from 0.5 – 1.5% wt per volume (paragraph 0038 and 0017). The formulation further comprises xanthan gum at 1.5% (Tables 1 and 4).

It is respectfully noted that the formulation of Tait is termed a stool marker, and that the formulation of Applicant is termed a contrast agent which is used in imaging an individual's anatomic segment. However, Tait clearly meets these limitations because the colon is imaged upon administration of the stool marker (paragraph 0026). Furthermore, it is noted that the recitation of the intended use has not been given patentable weight to distinguish over Tait in the respective product claims because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Tait discloses compositions that are the same as those claimed, they would be capable of performing the intended use, as claimed. Regarding claims 1 – 5, Tait *et al.* do not disclose a Hounsfield value, however the Hounsfield value is an inherent property of a given contrast agent, and in the absence of evidence to the contrary, the stated barium sulfate-containing contrast agent is of suitable concentration to be expected to have a Hounsfield value within the claimed ranges. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claims 1 – 8, 10 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Litt *et al.* (*Acad. Radiol*, 2001, 8, p. 377 – 383).

Litt discloses barium sulfate loaded agarose as an effective material for construction of multimodality imaging phantoms (abstract). The compositions contain 0.25% - 6% wt/vol. barium sulfate suspensions (page 378). It is noted that the recitation of the intended use of the instant compositions "for use in imaging an individual's anatomic segment" has not been given patentable weight to distinguish over Litt because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Since Litt discloses contrast materials comprising 0.25% barium sulfate (i.e. about 0.2%), Litt meets the claims.

Claims 62 – 64, 66, 68 – 70, 74, and 76 – 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Raptopoulos *et al.* (*Radiology*, 1987, 164, p.653-656).

Raptopoulos discloses the oral use of a 12.5% corn oil emulsion (COE) for abdominal CT in humans (page 653). Adequate gastric distention was achieved, and the entire stomach and duodenum were distended throughout examination. The colon was also clearly defined. The density of the lumen ranged between –20 and 15 CT units. The mural density ranged between 30 and 55 CT units before administration of the contrast material; after injection the mural density enhanced to a range of 60 to 100 CT units. The difference between the density of the GI wall and the lower density of the lumen and extraluminal space resulted in optimal mural contrast resolution (page 654). No "pseudotumors" were noted in the patients, and COE may be used to differentiate between intraabdominal tumors and duodenum or unopacified bowel loops. In addition, two mesenteric masses were clearly identified. COE allowed differentiation of cholelithiasis and located calcification in small intrauterine fibroid from the GI tract. In patients with intestinal venous stasis, the intestinal wall was markedly enhanced in the absence of mural thickening. Differentiation of fluid-density endometriomas, and large splenic, renal and ovarian cysts was observed (page 656).

Claims 1 – 10, 12, 15, 16, 19 – 22, 34 – 26, 29 – 45, 48, 62, 64 and 69 – 85 are rejected under 35 U.S.C. 102(e) as being anticipated by Lefere *et al.* (US 2005/0175542).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Lefere discloses a colonic residue tagging system, formulation, kit, and method for use in preparing an individual for a predetermined activity which requires tagging at least some colonic residue in a digestive tract such that a medically and/or diagnostically useful procedure can be performed on the digestive tract. The tagging is barium sulfate (paragraph 0027), and may be in doses from 0.1 to 100% w/v (paragraph 0031). The tagging agents may be combined with a sugar-based compound, viscosity agents, or gums (paragraph 0030). The sugar-based compound is preferably sorbitol present in an amount from 0.1% to about 3% by volume (paragraph 0040). The tagging agents are orally administered, and images of an individual's gastrointestinal tract (e.g. colon) may be screened for abnormalities (e.g. cancer)) (paragraph 0065).

It is respectfully noted that the formulation of Lefere is termed a tagging agent, and that the formulation of Applicant is termed a contrast agent which is used in imaging an individual's anatomic segment. However, Lefere clearly meets these limitations because the colon is imaged upon administration of the tagging agent (paragraph 0065). Regarding claims 1 – 5, Lefere *et al.* do not disclose a Hounsfield value, however the Hounsfield value is an inherent property of a given contrast agent, and in the absence of evidence to the contrary, the stated barium sulfate-containing contrast agent is of suitable concentration to be expected to have a Hounsfield value within the claimed ranges. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 10, 12 – 45, 48, 62, 64 and 69 – 85 are rejected under 35 U.S.C. 103(a) as being obvious over Tait (US 2001/0036442) in view of Lefere *et al.* (US 2005/0175542).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Tait discloses stool markers comprising 0.5 – 1.5% w/v barium sulfate and xanthan gum, as set forth above.

Tait does not teach sorbitol in his formulation.

Lefere discloses tagging agents comprising 0.1 – 100% w/v barium sulfate, gums, and sorbitol, as set forth above.

Lefere does not teach a specific concentration of xanthan gum in his formulation.

It would have been obvious to one of ordinary skill in the art to include sorbitol in the formulation of Tait, because both Tait and Lefere are drawn to barium sulfate-based stool markers or tagging agents for CT colography. One would have been motivated to do so, and would have had a reasonable expectation of success in formulating an effective stool marker/tagging agent in doing so, because Lefere specifically teaches that the inclusion of sugar-based compounds is beneficial for partially filling the small bowel with fluid increasing the total volume of contents in the small bowel, thus causing an increase in the peristaltic activity resulting in rapid transport of the tagging agent into the colon (paragraph 0038). It is noted that the formulation of Tait is termed a stool marker and that of Lefere is termed a tagging agent, while the claimed formulation is termed a contrast agent which is used in imaging an individual's anatomic segment. However, Tait and Lefere clearly meet these limitations because the colon is imaged upon administration of the stool marker or tagging agent.

Claims 1 – 7, 12, 15 – 27, 29 – 41, 45, 48, 62, 69, 70, 74, and 76 – 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falasch (DD 23830 (abstract)) in view of Nyman (*Acta Radiol. Diagn.*, 1984, 25, p. 121 – 124), in further view of Fuisz *et al.* (US 6,337,082).

Falasch discloses $BaSO_4$ suspensions for x-ray diagnostics which are stabilized with clay in aqueous solutions. Barium sulfate represents from 0.5 to 2.0% of the compositions. The compositions also contain from 3 – 6% clays, sweeteners and flavors. The compositions are inexpensive and provide good sedimentation stability, contrast properties and physiological acceptability (abstract). Regarding claims 1 – 5, 34 – 39, 45, 62, 69, 70 and 76 – 80, Falasch *et al.* do not disclose a Hounsfield value, however the Hounsfield value is an inherent property of a given contrast agent, and in the absence of evidence to the contrary, the stated barium sulfate-containing contrast agent is of suitable concentration to be expected to have a Hounsfield value within the claimed ranges. The Office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same functional characteristics of the claimed product. The burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 U.S.P.Q.2d 1302, 1303 (PTO Bd. Pat. App. & Int. 1993), *Ex parte Gray*, 10 USPQ2d 1922, 1923 (PTO Bd. Pat. App. & Int.) and *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977).

Falasch does not recite which anatomical segments are imaged with his x-ray contrast composition, and does not specifically teach xanthan gum or sorbitol in his formulation.

Nyman teaches E-Z-CAT, a dilute barium sulfate solution with suspending agents that prevent a too rapid sedimentation, which comprises sorbitol (an osmotic agent), vegetable gum (a stabilizing agent) and 1.7% barium sulfate for use in distending and imaging the gastrointestinal tract, including the colon (pages 121 and 122).

Nyman fails to recite a specific concentration of osmotic agent or stabilizing agent.

Fuisz discloses an x-ray contrast medium comprising barium sulfate, a gelling agent, such as xanthan gum, from 3% to 50%, and a sugar, such as sorbitol, from 10% to 20% (claims 1, 6 – 13 and 16 – 18).

Fuisz fails to recite a barium concentration.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide a contrast agent having 0.5% barium sulfate, stabilizing agents and osmotic agents (xanthan gum and sorbitol) within the claimed concentration ranges suitable for use in x-ray imaging because Falasch teaches x-ray compositions having the claimed barium sulfate concentration which are inexpensive and provide good sedimentation stability, contrast properties and physiological acceptability (abstract). It would have been obvious to substitute alternative stabilizing / osmotic agents such as gum and sorbitol in the formulations, and one would have been motivated to do so, because Nyman teaches that such ingredients aid in maintaining dilute barium sulfate in suspension, rather than to sediment or flocculate (page 123, right column). While Nyman does not teach the specific concentration of such agents, it would have been obvious to use concentrations such as 3% to 50% xanthan gum and from 10% to 20% sorbitol because Fuisz shows that such concentrations are known in the art to be appropriate for x-ray contrast agent formulations.

Claims 1 – 7, 12, 15, 17, 34 – 41, 45, 48, 62, 63, 65, 67, 69, 70, 74, 76 – 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falasch *et al.* (DD 23830 (abstract)) in view of Gore (*Am. J. Roentgenology*, 1984, 143, p. 279 – 284).

Falasch discloses $BaSO_4$ suspensions for x-ray diagnostics which are stabilized with clay in aqueous solutions. Barium sulfate represents from 0.5 to 2.0% of the compositions, as set forth above.

Falasch does not recite which anatomical segments are imaged with his x-ray contrast composition and which diseases may be diagnosed therewith.

Gore teaches the use of CT for differentiating between patients with Crohn's disease and ulcerative colitis (abstract). The contrast agent used by Gore is E-Z-CAT dilute barium sulfate suspension (page 280). Regarding claims 34, 40, 45 and 48, the method of imaging is CT examination and the colon is imaged. Regarding claims 62, 63 and 65, the presence of active ulcers, ulcerative colitis, Crohn's disease and/or enlarged lymph nodes were diagnosed (page 280 – 281). Regarding claim 69, narrowing of the lumen of the colon was observed (page 279 and 281). Regarding claim 70, the colon was distended for CT imaging (page 280).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a composition comprising 0.5 – 2% barium sulfate for imaging of the gastrointestinal tract, including the colon, and for differentiating between patients with Crohn's disease and ulcerative colitis because Falasch teaches that his 0.5% barium sulfate formulation is an x-ray contrast agent, and one would have been motivated to do so because Gore teaches a similar barium sulfate contrast agent is capable of achieving such activity.

Claims 1 – 10, 12, 15 – 27, 29 – 45, 48, 62, 69, 70, 74, 76 – 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falasch (DD 23830 (abstract)), in view of Nyman (*Acta Radiol. Diagn.*, 1984, 25, p. 121 – 124) and Fuisz *et al.* (US 6,337,082), in further view of Litt *et al.* (*Acad. Radiol*, 2001, 8, p. 377 – 383).

Falasch discloses $BaSO_4$ suspensions for x-ray diagnostics which are stabilized with clay in aqueous solutions. Barium sulfate represents from 0.5 to 2.0% of the compositions, as set forth above.

Falasch does not recite which anatomical segments are imaged with his x-ray contrast composition, and does not specifically teach about 0.2% barium sulfate, xanthan gum or sorbitol in his formulation.

Nyman teaches E-Z-CAT, a dilute barium sulfate solution with suspending agents that prevent a too rapid sedimentation, which comprises sorbitol (an osmotic agent), vegetable gum (a stabilizing agent) and 1.7% barium sulfate for use in distending and imaging the gastrointestinal tract, including the colon (pages 121 and 122).

Nyman fails to recite a specific concentration of osmotic agent or stabilizing agent.

Fuisz discloses an x-ray contrast medium comprising barium sulfate, a gelling agent, such as xanthan gum, from 3% to 50%, and a sugar, such as sorbitol, from 10% to 20% (claims 1, 6 – 13 and 16 – 18).

Fuisz fails to recite a barium concentration.

Litt discloses barium sulfate loaded agarose as an effective material for construction of multimodality imaging phantoms (abstract). The compositions contain 0.25% - 6% wt/vol. barium sulfate suspensions (page 378).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to provide a contrast agent having 0.5% barium sulfate, stabilizing agents and osmotic agents (xanthan gum and sorbitol) within the claimed concentration ranges suitable for use in x-ray imaging because Falasch teaches x-ray compositions having the claimed barium sulfate concentration which are inexpensive and provide good sedimentation stability, contrast properties and physiological acceptability (abstract). It would have been obvious to substitute a gum and sorbitol in the formulations, and one would have been motivated to do so, because Nyman teaches that such ingredients aid in maintaining dilute barium sulfate in suspension, rather than to sediment or flocculate (page 123, right column). While Nyman does not teach the specific concentration of such agents, it would have been obvious to use concentrations such as 3% to 50% xanthan gum and from 10% to 20% sorbitol because Fuisz shows that such concentrations are known in the art to be appropriate for x-ray contrast agent formulations. It would have been further obvious to utilize a slightly lower amount of barium sulfate in the formulations, such as 0.25% (i.e. about 0.2%) because Litt teaches that barium sulfate suspensions of said composition are capable of providing contrast for CT. Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active agent is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See *In re Russell*, 439 F.2d 1228 169 USPQ 426 (CCPA 1971). With these things in mind a skilled artisan would have been motivated to combine the formulation of Falasch with the teachings of Nyman, Fuisz and Litt in order to provide a stable x-ray contrast formulation.

Claims 1 – 10, 12, 15, 17, 34 – 41, 45, 48, 62, 63, 65, 67, 69, 70, 74 and 76 – 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Falasch *et al.* (DD 23830 (abstract)) in view of Gore (*Am. J. Roentgenology*, 1984, 143, p. 279 – 284), in further view of Litt *et al.* (*Acad. Radiol*, 2001, 8, p. 377 – 383).

Falasch discloses $BaSO_4$ suspensions for x-ray diagnostics which are stabilized with clay in aqueous solutions. Barium sulfate represents from 0.5 to 2.0% of the compositions, as set forth above.

Falasch does not recite which anatomical segments are imaged with his x-ray contrast composition and which diseases may be diagnosed therewith, and does not teach a composition comprising about 0.2% barium sulfate.

Gore teaches the use of CT for differentiating between patients with Crohn's disease and ulcerative colitis (abstract). The contrast agent used by Gore is E-Z-CAT dilute barium sulfate suspension (page 280). Regarding claims 34, 40, 45 and 48, the method of imaging is CT examination and the colon is imaged. Regarding claims 62, 63 and 65, the presence of active ulcers, ulcerative colitis, Crohn's disease and/or enlarged lymph nodes were diagnosed (page 280 – 281). Regarding claim 69, narrowing of the lumen of the colon was observed (page 279 and 281). Regarding claim 70, the colon was distended for CT imaging (page 280).

Litt discloses barium sulfate loaded agarose as an effective material for construction of multimodality imaging phantoms (abstract). The compositions contain 0.25% - 6% wt/vol. barium sulfate suspensions (page 378).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a composition comprising 0.5 – 2% barium sulfate for imaging of the gastrointestinal tract, including the colon, and for differentiating between patients with Crohn's disease and ulcerative colitis because Falasch teaches that his 0.5% barium sulfate formulation is an x-ray contrast agent, and one would have been motivated to do so because Gore teaches a similar barium sulfate contrast agent is capable of achieving such activity. It would have been further obvious to utilize a slightly lower amount of barium sulfate in the formulations, such as 0.25% (i.e. about

0.2%) because Litt teaches that barium sulfate suspensions of said composition are capable of providing contrast for CT. Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various pharmaceutical compositions having various amounts of the active agent is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. See *In re Russell*, 439 F.2d 1228 169 USPQ 426 (CCPA 1971). With these things in mind a skilled artisan would have been motivated to combine the formulation of Falasch with the teachings of Gore and Litt in order to provide a stable x-ray contrast formulation for gastrointestinal CT imaging.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER